Abstract

Background: Cancer is the most prevalent disease in the word and one of the leading causes of increased mortality that Gastric cancer, liver cancer, and breast cancer have the highest mortality rates. Dihydropyrimidinones (DHPMs) and imidazoles are heterocyclic compounds. A review on previous studies revealed that DHPM and imidazole derivatives possess several medicinal properties including antitumor activity. In this study we examined the cytotoxic effects and cell cycle analysis of DHPM and 2,4,5-triaryl imidazole derivatives on human cancer cell lines.

Methods: AGS, MCF-7, and HEPG2 cancer cell lines were treated by compounds and incubated for 24 hours. Cytotoxicity was examined by MTT assay and the IC_{50} values for each compound were determined. For Top-ranked compounds EB/AO staining was used for apoptotic cell detection and DAPI staining method was used to analysis of cell cycle by flow cytometry.

Results: Top-ranked compounds were identified by MTT assay. 2(IC_{50}=12.43±0.8uM), 4(IC_{50}=0.45±0.03uM) and 1(IC_{50}=3.7±0.2uM) were the most active compounds in AGS, MCF-7 and HEPG2 cells, respectively. These compounds also showed increase in apoptotic cells .The cell cycle analysis indicated the arrest of the cell cycle at G1 phase in AGS and HEPG2 cell lines, whereas compound 4 had no effect on cell cycle profile of MCF-7 cells.

Conclusion: Results indicated that DHPM derivatives containing phenyl substituent on carboxamide group were the most effective compounds on AGS and HEPG2 cell lines and thiazole ring in this position enhanced cytotoxicity against HEPG2 cell line. Between imidazole derivatives, 3-bromophenyl moiety on C2 position of imidazole ring elevated the cytotoxicity especially on MCF-7 cell lines.

Key words: Dihydropyrimidinone, Imidazole, cytotoxicity, Cell cycle, Apoptosis